Abstract Type : Oral
Abstract Submission No. : 1642

Diabetic nephropathy drives oxidative phosphorylation of kidney-resident macrophages

Peong Gang Park[1], Chaelin Kang[3], Dong Ki Kim[2], Yon Su Kim[2], Hee Gyung Kang[1], Seung Seok Han[2]
[1]Department of Pediatrics-Nephrology, Seoul National University Hospital, Korea, Republic of
[2]Department of Internal Medicine-Nephrology, Seoul National University College of Medicine, Korea, Republic of
[3]Department of Department of Biomedical Sciences, Seoul National University College of Medicine, Korea, Republic of

Objectives: Kidney-resident macrophages (KRMs) have a role in the maintenance of kidney immunological homeostasis. Their immunological signature may be affected by kidney or systemic disease status, but this issue has not been thoroughly evaluated particularly in human kidneys. Herein, we evaluated the diabetes nephropathy (DN)-driven change in transcriptomic signature of KRMs using human single-cell RNA sequencing dataset.

Methods: A total of 9 open-source databases containing 106 kidneys with 184,000 cells (n = 33,862 and 149,601 for DN and healthy kidneys, respectively) were merged to evaluate the transcriptomic profiling of KRMs. Gene set enrichment analysis was used to characterize biological process of KRMs in DN. A weighted correlation network analysis was applied to construct genetic modules of KRM subsets.

Results: A total of 959 cells were clustered for KRM with genetic markers, such as *C1QC*, *MRC1*, *CD68*, *CD14*, and *HLA-DRA*. Analysis with differentially expressed genes determined that oxidative phosphorylation pathway was highly enriched in KRMs from DN kidneys compared to those from healthy kidneys. Throughout network analysis, genes of KRMs were categorized into 5 modules. Among them, 3 modules were higher distributed in DN kidneys than healthy kidneys. Commonly upregulated pathway of KRM modules located in DN kidneys was also oxidative phosphorylation.

Conclusions: The signature of KRMs in DN kidneys is oxidative phosphorylation. This immunological shape of KRM may break surrounding parenchymal homeostasis and lead to unfavorable outcomes of DN.